

REMARKS

STATUS OF THE CLAIMS

Claims 1-13 and 15-24 are currently pending in this application. Claims 1-9 and 16-18 are withdrawn from consideration by the Examiner as allegedly drawn to non-elected subject matter. Claim 14 is canceled without prejudice or disclaimer. Claims 10-13, 15, and 19-24 are currently under examination.

FORMAL MATTERS

Applicants thank the Examiner for withdrawing the finality of the Office Action dated May 2, 2007, and for withdrawing all of the previous rejections of the claims.

REJECTIONS UNDER 35 U.S.C. § 112

Claims 10-13, 15, and 19-24 are rejected under 35 U.S.C. § 112 ¶ 1 as allegedly failing to comply with the enablement requirement. Office Action at pp. 2-4. Specifically, the Office cites *Heimburger V. N. et al.*, "Factor VIII Concentrate, Highly-Purified and Heated in Solution," *Drug Res.*, 31:619-622 (1981) ("*Heimburger*")¹ as allegedly demonstrating the unpredictability of the claimed invention. *Id.* Applicants respectfully traverse.

Despite taking into consideration the individual *Wands* factors, the Office's enablement rejection is based essentially on one main assertion:

¹ Applicants note the following minor errors in the English-language translation of the *Heimburger* article:

- Page 6: "spiking factor" should be "enrichment factor."
- Page 7: "spiking" should be "removal."
- Page 10: "factor VII" should be "factor VIII."

[T]he instant invention is unpredictable because the instant method claimed does not produce a concentrate in which the ratio of ristocetin to vWF is greater than 1 because the prior art reference teaches the same method steps produce a concentrate in which the ratio is less than 1. Thus, according to the method instantly claimed, it appears that steps to produce a concentrate of ristocetin to vWF greater than 1 are not claimed.

Office Action at p. 4. That assertion permeates the Office's enablement analysis. But, that analysis neglects to consider that the specification provides ample disclosure of the operability of the instant invention for producing a concentrate of a factor VIII:C-containing von Willebrand factor wherein the ratio of ristocetin cofactor activity to antigen is greater than 1.

First, Applicants would like to correct an apparent error in the Office's characterization of *Heimburger*. The Office states, "The prior art, Heimburger et al. . . . teaches a method that is the same as the instant method wherein a solution is fractionally precipitated using aluminum hydroxide (an alkali metal) and glycine." Office Action at p. 3. In fact, aluminum hydroxide is not an alkali metal salt. Applicants note, however, that *Heimburger* discloses precipitation of factor vWF/FVIII:C with sodium chloride, which is an alkali metal salt.

Notwithstanding, as the Office admits, *Heimburger* does not anticipate the currently pending claims and, therefore, does not teach the instant invention. Accordingly, *Heimburger's* failure to produce a vWF/FVIII:C concentrate in which the ratio of vWF:RCoF to vWF:Ag is greater than 1 does not reflect nonenablement of the claimed invention.

Inoperable embodiments are not encompassed by the currently pending claims. Furthermore, "a patent's claims need not specifically exclude possible inoperative substances in order to be enabled, unless 'the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention.'" *Ajinomoto Co. Inc. v. Archer-Daniels-Midland Co.*, 1996 WL 621837, at *16 (D. Del. 1996) (citing *Atlas Powder Co. v. E.I. duPont De Nemours*, 750 F.2d 1569, 1576 (Fed. Cir. 1984)) (emphasis omitted). The invention in *Atlas Powder* related to emulsion blasting agents. The specification listed numerous salts, fuels, and emulsifiers that could be used to form thousands of emulsions encompassed by the claim at issue, some of which were believed to be inoperable. However, the court held that the patent was enabling despite any inoperable embodiments because the specification provided sufficient guidance such that one skilled in the art could determine the proper combination of ingredients to limit the claims to operative embodiments.

Similarly, the instant specification provides ample guidance for selecting operable embodiments encompassed by claims 10-13, 15, and 19-24. Specifically, Applicants have discovered methods for fine-tuning the claimed process to adjust the ratio of vWF:RCoF to vWF:Ag in the concentrate product. For example, page 8, lines 6-16 teach, "[t]he adjustment of a particular concentration range of precipitants . . . makes it possible to shift the activity ratio in favor of a higher vWF:RCoF activity, this being the result of enrichment of high molecular weight vWF multimers." *Id.* Likewise, page 14, lines 29-31, teach that "precipitation depended not on the exposure times but primarily

on the glycine concentration," and page 22, lines 24-27 teach "a partitioning of the vWF multimers according to size can be achieved by appropriate adjustment of the equilibrium with NaCl and glycine." Finally, ranges of concentrations for the precipitants are provided on page 7, lines 29-32, and are recited in claim 13, and exemplary concentrations for the precipitants are provided in the Examples on pages 9-22 of the specification.

Moreover, the specification provides **ten** examples of operative embodiments of the invention:

- Example 1 on pages 9-11 and Table 1 on page 11;
- Example 2 on pages 9-14, Table 3 on page 13, and Table 4 on page 14;
- Example 4 on pages 16-18 and Table 8 on page 17; and
- Example 5 on pages 18-21 and Table 9 on page 21.

Accordingly, the specification demonstrates that the claimed invention is operable and enabled. Applicants respectfully submit that the single example of an inoperable embodiment disclosed in *Heimbürger* is insufficient to demonstrate that one of ordinary skill in the art would be forced "to experiment unduly in order to practice the claimed invention." *Ajinomoto*, 1996 WL 621837, at *16 (D. Del. 1996).

The seminal case of *In re Wands*, 858 F.2d 731, 737-8 provides a classic example of an enabled invention in a biotechnology field the court considered potentially unpredictable, that of a monoclonal antibody for a particular antigen. The court acknowledged in *Wands* that the methods required to make hybridoma cells at the time of the invention were complicated and time-consuming and that the outcome of screens

to find the claimed monoclonal antibodies would not be predictable. But, the court recognized that despite the unpredictability, hybridoma technology involves a series of routine procedures and that the specification provided sufficient directions for one to identify operable embodiments of the invention. The court's opinion emphasized that, even in an unpredictable art, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.* at 740 (citations omitted). Thus, the test for enablement is not quantitative, but rather, whether the experimentation required to practice the claimed invention is undue.
M.P.E.P. § 2164.06.

As in *Atlas Powder and Wands*, the instant specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed and exemplifies a sufficient number of operable embodiments to demonstrate the operability of the invention. Accordingly, claims 10-13, 15, and 19-24 are fully enabled by the specification.

In view of the foregoing discussion of the ample guidance provided by the specification, one skilled in the art could readily identify operable embodiments of the instantly claimed invention without undue experimentation. Accordingly, Applicants respectfully request that the enablement rejection of claims 10-13, 15, and 19-24 be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.


Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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